REMARKS

In view of the forgoing changes and following remarks, reconsideration and allowance are respectfully requested. Presently, claims 1-20 are pending, of which claims 17-20 stand withdrawn from consideration following a restriction requirement by the Examiner.

I. Objections to the Drawings and Specification

The Examiner has objected to the drawings and the specification. To clarify the issues with regard to the figures and the brief description of the drawings in the specification, Figures 1 and 2 have been cancelled and Figures 3 and 4 have been amended to renumber them Figures 1 and 2. The content of original Figures 1 and 2 have been incorporated into the specification as Tables 1 and 2. Such designations are consistent with the specification as originally filed. Further, Table 1 has been prepared to include sequence identifiers and base numbering.

As such, the specification now includes Tables 1 and 2, and the brief description of the drawings correspond to amended Figures 1 and 2. Further, the specification has been amended to update the status of the related applications. Accordingly, withdrawal of these objections is respectfully requested.

II. 35 U.S.C. § 101 Rejection

Claims 1 and 2 stand rejected under 35 U.S.C. § 101 because the claimed invention is allegedly directed to non-statutory subject matter. Claims 1 and 2 have been amended to claim an "isolated" nucleic acid molecule. As such, it is submitted that the claims comply with 35 U.S.C. § 101, and withdrawal of this rejection is respectfully requested.

III. 35 U.S.C. § 112, First Paragraph Rejection

Claims 2 and 3 stand rejected under 35 U.S.C. § 112, first paragraph as allegedly containing subject matter which Applicant did not have possession of at the time the application was filed. Specifically, the Examiner asserts that claims 2 and 3 read on the full length rpoB gene for which SEQ ID NOS. 2-10 do not provide adequate support. Claims 2 and 3 have been amended to clarify that the claims cover nucleic acid sequences selected from the group consisting of SEQ ID NOS. 2-10, rather than full length rpoB genes. As such, withdrawal of this rejection is respectfully requested.

IV. 35 U.S.C. § 112 , Second Paragraph Rejections

Claims 1-16 stand rejected under 35 U.S.C. § 112, second paragraph as allegedly being indefinite. Withdrawal of these rejections is respectfully requested for the reasons which follow.

A. Claims 1-14

Claims 1-14 stand rejected because it allegedly can not be determined whether the nucleic acids encompasses any one of the listed sequences, any part of the listed sequences, any combination of the listed sequences, or any sequence comprising any one of the listed sequences. The claims have been amended to recite proper Markush language. As such, it is submitted that one of skill would be apprised of the metes and bounds of the claims, and withdrawal of this rejection is respectfully requested.

B. Claims 2 and 3

Claims 2 and 3 stand rejected because the terms "complete" and "full length" are allegedly indefinite. The claims have been amended to remove such allegedly indefinite terms and to incorporate proper Markush language. As such, it is submitted that the claims comply with 35 U.S.C. § 112, second paragraph, and withdrawal of this rejection is respectfully requested.

C. Claim 3

Claim 3 stands rejected because it is allegedly unclear as to whether the set of probes refers to probes binding to each of the listed sequences, any port or combination of the listed sequences, or to a mixture of more than one probe that binds to any one of the listed sequences. Claim 3 has been amended to include proper Markush language and to claim a single probe. As such, it is submitted that the claims comply with 35 U.S.C. § 112, second paragraph, and withdrawal of this rejection is respectfully requested.

D. Claims 7-16

Claim 7-16 stand rejected due to the recitation of the term "highlighted regions". The claims have been amended to structurally define the highlighted regions of the claimed sequences. As such, it is submitted that the claims comply with 35 U.S.C. § 112, second paragraph, and withdrawal of this rejection is respectfully requested.

E. Claims 11-16

Claims 11-16 stand rejected because hybridization conditions are not specified and it is allegedly unclear how a probe hybridizes to SEQ ID NO 1, yet does not hybridize to SEQ

ID NO 1. The claims have been amended to recite that the probe hybridizes under stringent hybridization conditions. Such conditions are described in the specification on page 7, lines 12-17, and are generally known in the art. Further, the claims have been amended to recite that the probe hybridizes to SEQ ID NOS 2-10, but not to SEQ ID NO 1. As such, it is submitted that the claims comply with 35 U.S.C. § 112, second paragraph, and withdrawal of this rejection is respectfully requested.

F. Claims 6 and 10

Claims 6 and 10 stand rejected because it is allegedly unclear whether the claims cover the listed sequences or parts from any one or more of the listed sequences. The claims have been amended to incorporate proper Markush language. As such, it is submitted that the claims comply with 35 U.S.C. § 112, second paragraph, and withdrawal of this rejection is respectfully requested.

G. Claims 7-10

Claims 7-10 stand rejected due to the recitation of the term "corresponding position." The claims have been amended to clarify the meaning of the term and to provide for a reference sequence (i.e., SEQ ID NO 1) and a reference point (i.e., maximal alignment). As such, it is submitted that the claims comply with 35 U.S.C. § 112, second paragraph, and withdrawal of this rejection is respectfully requested.

V. 35 U.S.C. § 102 Rejections

A. De Beenhouwer et al.

Claims 1, 7, and 11-16 stand rejected under 35 U.S.C. § 102(b) as allegedly anticipated by De Beenhouwer et al. Reconsideration and withdrawal of this rejection are respectfully requested for the reasons which follow.

Claim 1, as amended, is directed to an isolated nucleic acid molecule comprising at least 300 contiguous bases of a sequence selected from SEQ ID NOS 2-10. De Beenhouwer does not disclose 300 contiguous bases of the claimed sequences. Likewise, claim 16 recites a probe or primer which hybridizes to at least 300 contiguous bases of the claimed sequences. As such, it is respectfully submitted that De Beenhouwer does not teach the invention of claims 1 and 16.

Further, claim 7, as amended, relates to a method for classifying a mycobacteria comprising comparing identified bases in a target sequence with at least one sequences selected from SEQ ID NOS 2-10. Again, De Beenhouwer does not disclose SEQ ID NOS 2-

10. As such, it is respectfully submitted that De Beenhouwer does not teach the invention of claim 7.

Claims 11-16, as amended, relate to a probe or primer that hybridizes under stringent hybridization conditions to at least a segment of a mycobacterial rpoB sequence selected from the group consisting of SEQ ID NOS: 2-10 or its complement without hybridizing to the M. tuberculosis sequence of SEQ ID NO: 1 or its complement, wherein the segment includes at least 20 bases of a sequence selected from the group consisting of SEQ ID NOS. 2-10 which differ from the corresponding one or more bases in SEQ ID NO 1 when the sequences are maximally aligned. De Beenhouwer does not disclose a sequence which includes at least 10 bases which differ from the corresponding bases in SEQ ID NO 1. As such, it is respectfully submitted that De Beenhouwer does not teach the invention of claims 11-16.

For at least these reasons, it is submitted that De Beenhouwer does not teach each and every limitation of the claims, and withdrawal of this rejection is respectfully requested.

B. Miller et al.

Claims 1 and 2 stand rejected under 35 U.S.C. § 102 (b) as allegedly anticipated by Miller et al. Reconsideration and withdrawal of this rejection are respectfully requested for the reasons which follow.

Miller teaches fragments of the complete rpoB sequence which is reported to be 100% complementary to SEQ ID NO 1. As described throughout the specification, SEQ ID NO 1 exemplifies a reference sequence from M. tuberculosis. As such, claims 1 and 2 have been amended to remove reference to SEQ ID NO 1. Accordingly, Miller does not disclose the presently claims sequences. For at least this reason, it is submitted that Miller does not teach each and every limitation of the claims, and withdrawal of this rejection is respectfully requested.

VI. 35 U.S.C. § 103 Rejections

A. Miller et al.

Claim 3 stands rejected under 35 U.S.C. § 103(a) as allegedly unpatentable over Miller et al. Reconsideration and withdrawal of this rejection are respectfully requested for the reasons which follow.

Miller teaches fragments of the complete rpoB sequence which is reported to be 100% complementary to SEQ ID NO 1, and probes that encompass the rpoB gene. However, Miller does not teach a probe that spans the full length of SEQ ID NO 1. Nonetheless, the

Examiner alleges that it would have been obvious to one of ordinary skill in the art to design such a probe.

As described throughout the specification, SEQ ID NO 1 exemplifies a reference sequence from M. tuberculosis. As such, claim 3 has been amended to remove reference to SEQ ID NO 1. Accordingly, Miller does not disclose the presently claimed sequences or provide any suggestion or motivation to one of skill in the art to modify the teachings of Miller to arrive at the present invention.. For at least this reason, it is submitted that Miller does not render claim 3 obvious, and withdrawal of this rejection is respectfully requested.

B. Telenti et al. in View of Miller et al.

Claims 4 and 5 stand rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Telenti et al. in view of Miller et al. Reconsideration and withdrawal of this rejection are respectfully requested for the reasons which follow.

Telenti teaches a method for detecting and classifying M. tuberculosis by their antibiotic resistance by a sequence comparison to M. tuberculosis H37v rpoB gene. However, Telenti does not explicitly teach any of the claimed sequences. Nonetheless, the Examiner relies on the disclosure of Miller to provide a teaching of SEQ ID NO 1 and asserts that it would have been obvious to one of ordinary skill in the art to combine the teachings of Telenti and Miller.

Again, claims 4 and 5 have been amended to remove reference to SEQ ID NO 1. As such, it is submitted that neither Telenti nor Miller teach or suggest any of the presently claims sequences. As such, one of skill in the art would not be motivated to modify the teachings of Telenti and Miller to arrive at the present invention. For at least this reason, it is respectfully submitted that the claims are patentable over Telenti and Miller, and withdrawal of this rejection is respectfully requested.

C. De Beenhouwer

Claims 8-10 stand rejected under 35 U.S.C. § 103(a) as allegedly unpatentable over De Beenhouwer. Reconsideration and withdrawal of this rejection are respectfully requested for the reasons which follow.

De Beenhouwer teaches a method for detecting and identification of mycobacterium species. Further, De Beenhouwer teaches an *M. avian* ITG 5887 rpoB sequence which contains 267 contiguous base pairs that are 100% complementary to SEQ ID NO 7 of the present invention. However, the Examiner states that De Beenhouwer does not explicitly teach the identification of at least 10 "highlighted" bases in determining species

characterization. Nonetheless, the Examiner asserts that it would have been obvious to one of ordinary skill in the art to use the disclosed *M. avium* ITG 5887 rpoB sequence in order to identify *M avium* strains, to design probes that would contain the highlighted regions, and to provide a comparison with other sequences from isolates in order to identify the *M. avium* strain.

First, as mentioned above, independent claim 7, as amended, relates to a method for classifying a mycobacteria comprising comparing identified bases in a target sequence with at least one sequences selected from SEQ ID NOS 2-10. Again, De Beenhouwer does not disclose SEQ ID NOS 2-10. As such, it is respectfully submitted that De Beenhouwer does not teach the invention of claim 7 or dependent claims 8-10.

Further, absent a teaching of the importance of the highlighted regions of the claimed sequences, it is submitted that one of skill in the art would have no motivation to specifically design probes that would contain at least 10, much less 20 of the highlighted bases. As such, it appears as though the Examiner is relying on improper hindsight reasoning to arrive at the present invention from the teaching of De Beenhouwer. For at least these reasons, it is respectfully submitted that the claims are patentable over De Beenhouwer, and withdrawal of this rejection is respectfully requested.

CONCLUSION

Accordingly, Applicant submits that the present claims are in condition for allowance and notification of such is respectfully requested. If the Examiner has any question, please contact the undersigned so that a personal interview can be scheduled.

Respectfully submitted,
PILLSBURY WINTHROP, LLP

By Mulan M Unnda 45,979
for Paul N. Kokulis
Reg. No. 16,773

1600 Tysons Boulevard
McLean, VA 22102
Tel No: (703) 905-2000
Fax No.: (703) 905-2500

APPENDIX

VII. VERSION WITH MARKINGS TO SHOW CHANGES MADE

IN THE SPECIFICATION:

In the specification on page 1, the whole paragraph starting at line 13 is deleted and replaced with the following new paragraph.

This application derives priority from USSN 60/080,616, filed April 3, 1999, now abandoned, [and] which is incorporated by reference. Further, Applications 08/797,812, filed February 7, 1997, now US Patent 6,228,575; USSN 60/011,339, filed 08 Feb. 1996, now abandoned; 60/012,634, filed 01 March 1996, now abandoned; 08/629,031, filed 08 April 1996, currently pending; and 60/017,765, filed 15 May 1996, now abandoned, are directed to related subject matter. These applications are specifically incorporated by reference in their entirety for all purposes.

New pages 21-73 are entered.

IN THE CLAIMS:

The claims are amended as follows:

1. (Three Times Amended) An isolated nucleic acid molecule comprising at least [50] 300 contiguous bases from an rpoB sequence [designated as any of the] selected from the group consisting of SEQ ID NOS: [1-10] 2-10.

2. (Three Times Amended) The isolated nucleic acid molecule of claim 1 comprising a [complete] rpoB sequence [designated as any of the] selected from the group consisting of SEQ ID NOS: [1-10] 2-10.

3. (Three Times Amended) A [set of probes] probe perfectly complementary to [and spanning a full-length sequence designated as of the] a rpoB sequence selected from the group consisting of SEQ ID NOS: [1-10] 2-10.

4. (Three Times Amended) A method of classifying a mycobacteria, comprising

providing a sample comprising a mycobacterial rpoB target nucleic acid from a mycobacteria;

determining the sequence of a segment of at least 50 contiguous bases from the target nucleic acid;

comparing the determined sequence to at least one sequence [designated as] selected from the group consisting of SEQ ID NOS: [1-10] 2-10;

classifying the mycobacteria from the extent of similarity of the compared sequences.

6. (Three Times Amended) The method of claim 4, wherein the determined sequence is compared with at least [ten] nine sequences [designated as] selected from the group consisting of SEQ ID NOS: [1-10] 2-10.

7. (Three Times Amended) A method of classifying a mycobacteria, comprising

providing a sample comprising a mycobacterial rpoB target nucleic acid;

determining the identity of one or more bases in the target sequence at one or more positions corresponding to one or more [of the highlighted positions] bases in a sequence [designated as any of the] selected from the group consisting of SEQ ID NOS: [1-10] 2-10 when the sequences are maximally aligned, wherein the one or more bases of the sequence selected from the group consisting of SEQ ID NOS. 2-10 differ from the corresponding one or more bases in SEQ ID NO 1 when the sequences are maximally aligned, the identity of the one or more bases characterizing the species of mycobacteria that is present in the sample;

comparing the identified one or more bases in the target sequence to at least one sequence selected from the group consisting of SEQ ID NOS: 2-10;

classifying the mycobacteria from the extent of similarity between the one or more bases identified in the target sequence and the corresponding one or more bases in the compared sequences.

8. (Three Times Amended) The method of claim 7, wherein the identity of at least 10 bases in the target nucleic acid at positions corresponding to [highlighted positions] the one or more bases in [a] the sequence [designated as any of the] selected from the group consisting of SEQ ID NOS: [1-10] 2-10 is determined.

9. (Twice Amended) The method of claim 8, wherein the identity of at least 20 bases in the target sequence at [highlighted positions] positions corresponding to the one or more bases in the sequence [designated as any of the] selected from the group consisting of SEQ ID NOS: [1-10] 2-10 are identified.

10. (Three Times Amended) The method of claim 9, further comprising comparing the 20 determined bases with 20 bases occupying corresponding positions in each of at least [ten] nine sequences [designated as any of the] selected from the group consisting of SEQ ID NOS: [1-10] 2-10.

11. (Three Times Amended) A sequence-specific polynucleotide probe or primer that hybridizes under stringent hybridization conditions to at least a segment of a mycobacterial rpoB sequence [designated as any of the] selected from the group consisting of SEQ ID NOS: [1-10] 2-10 or its complement without hybridizing to the M. tuberculosis sequence [designated] of SEQ ID NO: 1 or its complement, wherein the segment includes [a highlighted nucleotide position designated as any of the SEQ ID NOS: 1-10] at least 20 bases of a sequence selected from the group consisting of SEQ ID NOS. 2-10 which differ from the corresponding bases in SEQ ID NO 1 when the sequences are maximally aligned.

13. (Four Times Amended) The sequence-specific polynucleotide of claim 12, wherein a central position of the probe aligns with [a highlighted nucleotide position designated as any of the SEQ ID NOS: 1-10] the one or more bases of a sequence selected from the group consisting of SEQ ID NOS. 2-10 which differ from the corresponding one or more bases in SEQ ID NO 1 when the sequences are maximally aligned.

15. (Four Times Amended) The sequence-specific polynucleotide of claim 14, wherein the 3' end of the primer aligns with [a highlighted nucleotide position designated as any of the SEQ ID NOS: 1-10] the one or more bases of a sequence selected from the group consisting of SEQ ID NOS. 2-10 which differ from the corresponding one or more bases in SEQ ID NO 1 when the sequences are maximally aligned.

16. (Twice Amended) The sequence-specific polynucleotide of claim 11 [that is between 10 and 50 bases long] that hybridizes under stringent hybridization conditions to at least 300 contiguous bases of a mycobacterial rpoB sequence selected from the group consisting of SEQ ID NOS: 2-10 or its complement without hybridizing to the M. tuberculosis sequence of SEQ ID NO: 1 or its complement.